

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/010844

International filing date (day/month/year)
23.09.2004

Priority date (day/month/year)
27.09.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4706, C07D215/54, C07D405/12, C07D401/12, C07D401/14, C07D405/14, A61K31/4709, A61P29/00,

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/010844

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 15 (with respect to industrial applicability)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 15
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/010844

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-19 No: Claims
Inventive step (IS)	Yes: Claims 1-19 No: Claims
Industrial applicability (IA)	Yes: Claims 1-14;16-19 No: Claims

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 15 relates to subject-matter considered by this Authority to be covered by the provision of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

- D1: WO 97/44322 A (MONTANA JOHN GARY ; DYKE HAZEL JOAN (GB); CHIROSCIENCE LTD (GB)) 27 November 1997 (1997-11-27)
Do: WO 02/20489 A (SQUIBB BRISTOL MYERS CO ; YU GUIXUE (US); BI YINGZHI (US); MACOR JOHN) 14 March 2002 (2002-03-14)
D3: WO 02/092571 A (ASTRAZENECA AB ; LARSSON JOAKIM (SE); SJOE PETER (SE)) 21 November 2002 (2002-11-21)

2. Novelty (Article 33(1) and (2) PCT)

The subject-matter of the present application relates to compounds of formula (I) (see present Claim 1) as PDE4 inhibitors. The present compounds are novel over the compounds disclosed by D1-D3 on the account of the present specific substituents from the position 3-, 4- and 6- of the quinoline ring. Consequently, the novelty of the present subject-matter is acknowledged.

3. Inventive step (Article 33(1) and 33(3) PCT)

The present subject-matter relates to compounds of formula (I) as PDE4 inhibitors, useful as medicament for treating inflammatory and/or allergic diseases.

D1, which is regarding as the closest prior art, discloses 5-sulphonamide-quinolines as PDE4 inhibitors, useful to treat the same disease as in the present case (see Claims 1, 13 and 17). The compounds disclosed by D1 are not specific

substituted either in position 3 with a carboxamide function or in position 4 with an amino derivative as in the present case.

The technical problem of the present application may therefore be regarded as a provision of further quinoline derivatives as PDE4 inhibitors.

D2 discloses quinoline derivatives of formula (I) (see Claim 1) as PDE inhibitors especially as PDE5 inhibitors (see pages 27-33). The compounds disclosed by D2 do not bear any sulphonamide function as in the present case and moreover the amino function from the position 4-th of the quinoline ring is not substituted with a directly linked aryl (see e.g. examples 59-64).

D3 discloses 4-anilinoquinolin-3-carboxamides as JAK3 kinase inhibitors, useful to treat inflammatory, immunological and bronchopulmonary diseases (see page 10). The compounds disclosed by D3 can be substituted in position 6 of the core-structure with different substituents R1, but none of them is a sulphonamide function (see the definition of R1 for the compounds claimed by the present Claim 1).

Since none of the cited prior art documents discloses, either alone or in combination, the possibility for PDE4 inhibitors to be substituted in position 3-, 4- and 6- of the quinoline ring with the specific present moieties an inventive step can be acknowledged for the present subject-matter.

4. Industrial applicability (Article 33(4)PCT).

For the assessment of the present claim 15 on the question whether they are industrial applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may also allow, however, claims to a known compound for the manufacture of a medicament for a new medical treatment.